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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,803	09/17/2003	Thomas Lengsfeld	06478.1493	3763
7590 09/14/2005 Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P. 1300 I Street, N.W. Washington, DC 20005-3315			EXAMINER MCKANE, ELIZABETH L	
			ART UNIT 1744	PAPER NUMBER

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/663,803

Applicant(s)

LENGSFELD ET AL.

Examiner

Leigh McKane

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>091703.112503</u> . | 6) <input type="checkbox"/> Other: _____ |

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-4, 17, 18, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaev et al (US 2001/0049354) in view of Kumar et al ("Free radical scavenging activity of vanillin and *o*-vanillin using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical").

With respect to claims 1, 3, 4, 20-22, Shalaev et al teaches a method of sterilizing a

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protein containing pharmaceutical composition wherein the composition is contacted with *o*-vanillin and irradiated with ionizing radiation, including electromagnetic radiation (gamma). See paragraphs [0003], [0011], [0014], [0016], and [0017]. Shalaev et al is silent with respect to contacting the protein-containing composition with vanillin, the positional isomer of *o*-vanillin.

Kumar et al discloses that it was known in the art at the time of the invention that vanillin, as well as *o*-vanillin, is a powerful free radical scavenger, and has been shown to inhibit formation of DNA single strand breaks induced by singlet oxygen and to inhibit singlet oxygen-induced protein oxidation. See pages 35-36, "Introduction."

As both vanillin and *o*-vanillin have been shown to be effective in scavenging free radicals in biological/protein compositions, it would have been obvious to one of ordinary skill in the art to use vanillin in place of *o*-vanillin in the method of Shalaev et al, since one would have expected vanillin to be effective in protecting the protein composition from radiation-induced free radical damage.

With respect to claim 2, Shalaev et al discloses that the protein composition is *sterilized*. Use of the term sterilization implies the complete destruction of all viruses. Therefore, the step of irradiation taught by Shalaev et al would have achieved a 4 log reduction of all viruses.

As to claims 17 and 18, Kumar et al teaches that vanillin is effective in scavenging free radicals at millimolar concentrations. See page 39, lines 9-10. It is deemed obvious to optimize the concentration of vanillin dependent upon the particular protein composition and the desired outcome, as concentration is a result effective variable ordinarily determinable by routine experimentation.

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5. Claims 8-11, 15, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaev et al and Kumar et al as applied to claim 1 above, and further in view of Chin et al (“Virucidal Short Wavelength Ultraviolet Light Treatment of Plasma and Factor VIII Concentrate: Protection of Proteins by Antioxidants.”).

With respect to claims 8-11, Shalaev et al teaches that the protein can be a blood product (paragraph [0014]) but does not specify a purified plasma protein. Chin et al discloses use of electromagnetic radiation (UVC at 254 nm) to sterilize plasma proteins wherein the protein is contacted, before irradiation, with a free radical scavenger. See page 4331, “Materials and Methods”. Suitable proteins include Factor VIII (page 4332, “Results”). It would have been obvious to employ the method of Shalaev et al with Kumar et al to sterilize other blood products, such as plasma proteins (Factor VIII), since electromagnetic radiation has been shown to be effective and safe in sterilizing these types of protein.

As to claims 15 and 16, while Shalaev et al is silent with respect to an additional virucidal method, Chin et al discloses that it was known in the art at the time of the invention to use two types of virucidal methods when sterilizing proteins – one which is effective against enveloped viruses (solvent/detergent) and a second which is effective against nonenveloped viruses (electromagnetic radiation). See page 4331, first two paragraphs. As electromagnetic radiation is effective against only nonenveloped viruses, it would have been obvious to add an additional virucidal treatment (solvent/detergent) to the method of Shalaev et al in order to inactivate all viruses in the protein composition.

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6. Claims 1-18 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chin et al in view of Kumar et al.

With respect to claims 1-11, 15, 16, and 20-22, Chin et al discloses a method of sterilizing plasma proteins using electromagnetic radiation (UVC at 254 nm) wherein the protein is contacted, before irradiation, with a free radical scavenger. See page 4331, "Materials and Methods". Suitable proteins include Factor VIII (page 4332, "Results"). Chin et al also teaches that it was known in the art at the time of the invention to use two types of virucidal methods when sterilizing proteins – one which is effective against enveloped viruses (solvent/detergent) and a second which is effective against nonenveloped viruses (electromagnetic radiation). See page 4331, first two paragraphs. The method of Chin et al achieves a greater than 10^5 reduction in nonenveloped viruses (Abstract). A solvent/detergent step removed enveloped viruses (page 4331, "Materials and Methods"). Chin et al is silent with respect to using vanillin as the free radical scavenger. Kumar et al discloses that it was known in the art at the time of the invention that vanillin is a powerful free radical scavenger, and has been shown to inhibit formation of DNA single strand breaks induced by singlet oxygen and to inhibit singlet oxygen-induced protein oxidation. See pages 35-36, "Introduction." It would have been obvious to one of ordinary skill in the art to substitute vanillin for the free radical scavengers used by Chin et al since vanillin has been shown by Kumar et al to be an effective free radical scavenger and because the method of Chin et al is not limited to a particular free radical scavenger.

As to claims 12-14, the combination of Chin et al with Kumar et al teaches the instant method and therefore would be intrinsically capable of achieving the claimed level of biological activity and percentage of aggregates.

With respect to claims 17 and 18, Kumar et al teaches that vanillin is effective in scavenging free radicals at millimolar concentrations. See page 39, lines 9-10. It is deemed obvious to optimize the concentration of vanillin used in the combination with Chin et al, dependent upon the particular protein composition and the desired outcome, as concentration is a result effective variable ordinarily determinable by routine experimentation.

7. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chin et al and Kumar et al as applied to claim 11 above, and further in view of Laub et al (US 2001/0046450).

Chin et al does not teach sterilizing of von Willebrand factor. Laub et al, however, evidences that it was known in the art at the time of the invention to sterilize blood products, including Factor VIII and von Willebrand factor, using a UVC radiation. See paragraph [0032]. Moreover, Laub et al discloses the use of free radical scavengers in combination with the UVC to protect the protein. See paragraph [0062].

It would have been obvious to one of ordinary skill in the art to employ the method of Chin et al to sterilize other plasma proteins, such as von Willebrand factor, since Laub et al teaches that the combination of UVC and a free radical scavenger is a safe and effective means of sterilizing blood products.

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kumar et al (abstract of "Effect of vanillin on methylene blue plus light-induced single

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strand breaks in plasmid pBR322 DNA”) teaches that vanillin is effective in scavenging singlet oxygen.

Okada et al (abstract of “The trapping capacity for free radicals of biologically related substances”) discloses the vanillin is an effective free radical scavenger.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh McKane whose telephone number is 571-272-1275. The examiner can normally be reached on Monday-Wednesday (5:30 am-3:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Leigh McKane
Primary Examiner
Art Unit 1744

elm
12 September 2005